UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/042,312	01/11/2002	Kanji Yahiro	2001_1892A	4407

513 7590 03/28/2005

WENDEROTH, LIND & PONACK, L.L.P.
2033 K STREET N. W.
SUITE 800
WASHINGTON, DC 20006-1021

EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 03/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/042,312	YAHIRO, KANJI	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8-11 and 13-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,8-11 and 13-15* is/are rejected.

7)☒ Claim(s) *5,10 and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submissions, filed 9/27/04 and 12/20/04, have been entered.

Amended claims 1, 5, 6, 10, 11, and 15, filed 12/20/04, are acknowledged.

Claims herein under examination are 1, 3-6, 8-11, and 13-15.

Claim Objections

Claims 5, 10, and 15 are objected to because of the following informalities:

These claims recite the phrase "data includes" which is improper grammar. Because "data" is in the plural form, its modifying verb must also be in the plural form.

Appropriate correction is requested.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-6, 8-11, and 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (lines 7 and 10), 3 (line 2), 4 (line 3), 6 (line 7), 8 (line 2), 9 (line 3), 11 (line 9), 13 (line 2), and 14 (lines 2-3) recite the phrase "the image" and/or "the image of the biological sample" which lack clear antecedent basis. It is unclear if "the image" is referring to image of the original biological sample or to the image of the biological sample with a deleted linear structure. Claims 5, 10, and 15 are also rejected due to their dependency from claims 1, 6, and 11.

Claim 1 (line 8), 6 (line 8), and 11 (line 10) recite the phrase "as a number of somas" which renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). The term "as" is defined as "for instance", according to the online Merriam-Webster dictionary, which is indefinite. Clarification of this issue via clearer claim wording is requested. Claims 3-5, 8-10, and 13-15 are also rejected due to their dependency from claims 1, 6, and 11.

Claim 1 recites an evaluation apparatus with three units (a condition pass/fail determining unit, a digitization unit, and a measuring area changing unit) which lack clarity. It is unclear if the units are intended to be structural units or if these units are intended to be part of a computer program. Clarification of this issue via clearer claim wording is requested. Claims 3-5 are also rejected due to their dependency from claim 1.

Claim 14 (line 2) recites the phrase "the predetermined value" the limitation. There is insufficient antecedent basis for this limitation in the claim. Correction is suggested by changing the term "the" to "a".

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, and 4 are under 35 U.S.C. 102(b) as being anticipated by Wilhelm et al. (P/N 5,715,327).

Due to the unclarity of whether the claimed evaluation apparatus contains units that are structural features or are computer program units, the following rejection is based on the interpretation of the units being structural in nature. Therefore, all of the intended uses listed in the preamble and body of claim 1 do not hold patentable weight and are not required to be present in the prior art, because these intended uses do not result in any structural difference with regard to the apparatus found in the prior art.

Wilhelm et al. disclose an evaluation apparatus for determining whether a slide containing a biological sample is suitable for processing (abstract). Wilhelm et al. disclose taking an image of the biological sample on the slide, processing the slide, determining whether the slide is suitable based on parameters, and whether a threshold (predetermined condition) has

been exceeded as well as suitability tests performed by an automated microscope system (Figure 2 and col. 1, lines 31-33) which represents the condition pass/fail determining unit, as stated in instant claim 1. Wilhelm et al. disclose tests performed by the system to quantify measurements including staining measures of means, ratios, counts of saturated pixels within images, percentage of images focused properly or improperly (col. 1, lines 35-47) which represents a digitization unit as well as a measuring area changing unit, as stated in instant claim 1. Wilhelm et al. disclose the biological sample includes a cell and the parameters (predetermined conditions) including cell ratios (cell numbers) and rings around the cell nuclei (area of the cell), mean nuclei stain, mean cytoplasm stain, and mean contrast between nuclei and cytoplasm (representing entire cell area) (abstract, Figure 4, and col. 1, lines 35-47). In Figure 1A, Wilhelm et al. disclose a calibration slide 524 (reference image). Wilhelm et al. disclose detecting intermediate cell ratios and reference cell ratios (col. 2, line 22) which are reasonably interpreted as a reference image compared to the test slide in the measuring area, as stated in instant claim 3. Wilhelm et al. disclose a slide suitability score which results from analyses applied to measurements of the slide's characteristics and an automated cytology system's effectiveness (col. 1, lines 10-12), which represent predetermined values resulting from a comparison between the test slide image and the reference slide image, as stated in instant claim 4. Wilhelm et al. disclose the apparatus includes an imaging system, a motion control system (measuring area changing unit), an image processing system (condition determining unit and digitizing unit), a central processing system, and a workstation (col. 3, lines 49-52 and col. 4, lines 23-26 and 37-42). Wilhelm et al. disclose the motor drivers position the slide under the optics (col. 4, line 9) and that measurements are taken on requested fields of view (col. 1, lines 17-18) so that the

motor driver is reasonably interpreted to be a measuring changing unit that changes the measuring area, as stated in instant claim 1.

Wilhelm et al. disclose a hard disk (col. 4, line 17) that represents a storage medium. Wilhelm et al. disclose the processes are implemented in software (computer program for executing a digital processor) (col. 4, lines 33-37). Wilhelm et al. disclose a central computer that controls the microscope and processor to acquire and digitize images from the microscope (col. 4, lines 23-26). The computer controls the microscope stage to position the specimen where one to fifteen field of view processors receive images (col. 4, lines 28-32). Wilhelm et al. disclose the flatness of the slide may be checked prior to slide suitability testing (col. 4, lines 23-32) which represents a determination if the slide conforms to a predetermined condition, as stated in instant claim 1. The processor computes a suitability score that indicates whether a slide has passed or failed (condition pass/fail determining unit) in any one of the thirteen suitability tests, as stated in instant claim 1. Wilhelm et al. disclose creating an image of the slide, measuring a suitability parameter, and then checking if the parameter exceeds a predetermined threshold (col. 5, lines 28-34) which represents a condition being previously set and judging whether the measuring area (image) conforms to the condition. Wilhelm et al. disclose a slide must pass all tests in order to be suitable for reporting results (col. 4, lines 39-40) which represents acquisition of data judged to conform to the condition. Therefore, if a slide does not pass all tests, then processing is considered unsuitable and result processing must cease (col. 4, lines 39-40 and col. 5, lines 24-27 and 40-44) which means that the measuring area does not conform and will no longer be considered which is reasonably interpreted to be a change in the measuring area performed by the automated microscope system. Wilhelm et al. disclose a

performance requirement of scoring no more than 5% of the training slides as being unsuitable (col. 5, lines 24-27), which represents use of more than one slide such that stopping the processing of a slide and proceeding processing with another slide clearly represents a changing in position of the measuring area with regard to the biological sample. Wilhelm et al. disclose clinicians using normal detected cells as reference cells against which all other cells on the slide can be compared (col. 5, lines 52-54).

Thus, Wilhelm et al. anticipate the limitations in claims 1, 3, and 4.

Applicant states Wilhelm et al. do not disclose a condition pass/fail determining unit as stated in instant claim 1. This statement is found unpersuasive as the evaluation apparatus of instant claim 1 has been interpreted to include 3 structural units such that the intended uses bear no patentable weight. Wilhelm et al. disclose a structural condition pass/fail determining unit, as discussed in the rejection above. Applicant describes the Wilhelm et al. invention. Applicant states that Wilhelm et al. fail to disclose that the central computer "deletes a linear structure of a cell having the linear structure extending from a main body of a soma from an image of a biological sample and determines whether a measuring area set as a numerical data acquiring area in the image of the biological sample has a number of main bodies, as a number of somas, that meets, a predetermined condition for acquiring numerical data". This statement is found unpersuasive as this limitation is considered to be an intended use in the structure limitation of the condition pass/fail determining unit that bears no patentable weight when the units in instant claim 1 are interpreted to be structural units. This lack of patentable weight is because the

intended use does not appear to result in any structural difference from what is found in the prior art.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-6, 8-11, and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilhelm et al. (P/N 5,715,327) in view of Sammak et al. (US 2001/0041347).

It is noted that support in the specification (page 8, line 13), figures, and claims as originally filed state that either length or area of the linear structure is obtained as numerical data, not both, as stated in instant claims 5, 10, and 15.

Wilhelm et al. describe a method performed on an automated microscope system and evaluation apparatus for determining whether a slide containing a biological sample is suitable for processing (abstract). Wilhelm et al. describe taking an image of the biological sample on the slide, processing the slide, determining whether the slide is suitable based on parameters, and whether a threshold (predetermined condition) has been exceeded (Figure 2) which represents setting a condition for acquiring the numerical data from a measuring area in an image to be evaluated, as stated in the setting step of instant claims 6 and 11. Wilhelm et al. describe the biological sample includes a cell and the parameters (predetermined conditions) including cell

ratios (cell numbers) and rings around the cell nuclei (area of the cell), mean nuclei stain, mean cytoplasm stain, and mean contrast between nuclei and cytoplasm (representing entire cell area) (abstract, Figure 4, and col. 1, lines 35-47). In Figure 1A, Wilhelm et al. describe a calibration slide 524 (reference image). Wilhelm et al. describe detecting intermediate cell ratios and reference cell ratios (col. 2, line 22) which are reasonably interpreted as a reference image compared to the test slide in the measuring area, as stated in instant claims 3, 8, and 13. Wilhelm et al. describe a slide suitability score which results from analyses applied to measurements of the slide's characteristics and an automated cytology system's effectiveness (col. 1, lines 10-12), which represent predetermined values resulting from a comparison between the test slide image and the reference slide image, as stated in instant claims 4, 9, and 14.

Wilhelm et al. describe the apparatus includes an imaging system, a motion control system (measuring area changing unit), an image processing system (condition determining unit and digitizing unit), a central processing system, and a workstation (col. 3, lines 49-52 and col. 4, lines 23-26 and 37-42). Wilhelm et al. describe the motor drivers position the slide under the optics (col. 4, line 9) and that measurements are taken on requested fields of view (col. 1, lines 17-18) so that the motor driver is reasonably interpreted to be a measuring changing unit that changes the measuring area, as stated in instant claim 1. Wilhelm et al. describe a hard disk (col. 4, line 17) that represents a storage medium, as stated in instant claims 11 and 13-15. Wilhelm et al. describe the processes are implemented in software (computer program for executing a digital processor) (col. 4, lines 33-37). Wilhelm et al. describe a central computer that controls the microscope and processor to acquire and digitize images from the microscope (col. 4, lines 23-26). The computer controls the microscope stage to position the specimen where one to fifteen

field of view processors receive images (col. 4, lines 28-32). Wilhelm et al. describe the flatness of the slide may be checked prior to slide suitability testing (col. 4, lines 23-32) which represents a determination if the slide conforms to a predetermined condition, as stated in instant claim 1. The processor computes a suitability score that indicates whether a slide has passed or failed (condition pass/fail determining unit) in any one of the thirteen suitability tests, as stated in instant claim 1. Wilhelm et al. describe creating an image of the slide, measuring a suitability parameter, and then checking if the parameter exceeds a predetermined threshold (col. 5, lines 28-34) which represents a condition being previously set and judging whether the measuring area (image) conforms to the condition, as stated in instant claims 6 and 11. Wilhelm et al. describe a slide must pass all tests in order to be suitable for reporting results (col. 4, lines 39-40) which represents acquisition of data judged to conform to the condition, as stated in the acquiring step of instant claims 6 and 11. Therefore, if a slide does not pass all tests, then processing is considered unsuitable and result processing must cease (col. 4, lines 39-40 and col. 5, lines 24-27 and 40-44) which means that the measuring area does not conform and will no longer be considered which is reasonably interpreted to be a change in the measuring area performed by the automated microscope system, as stated in instant claims 6 and 11. Wilhelm et al. describe a performance requirement of scoring no more than 5% of the training slides as being unsuitable (col. 5, lines 24-27), which represents use of more than one slide such that stopping the processing of a slide and proceeding processing with another slide clearly represents a changing in position of the measuring area with regard to the biological sample. Wilhelm et al. describe clinicians using normal detected cells as reference cells against which all other cells on the slide can be compared (col. 5, lines 52-54). Wilhelm et al. do not describe the biological sample as a

cell having a linear structure extending from a main body of a soma, deleting the linear structure from the sample image, or the numerical data including either a length or an area of the linear structure. One definition of "soma" is cell body that is defined on the online Merriam-Webster Dictionary as the nucleus-containing central part of a neuron exclusive of its axons and dendrites.

Sammak et al. describe automated systems, methods, screens, and software for the analysis of cell spreading via measurements calculated from cell images (abstract) which represents acquiring numerical data from measuring areas, as stated in the acquiring step of instant claims 6 and 11. Sammak et al. describe cells that include proteins that label microtubules fused to a luminescent protein. As the Merriam-Webster Dictionary defines microtubules as "any of the minute tubules in eukaryotic cytoplasm that are composed of the protein tubulin and form an important component of the cytoskeleton", Sammak et al. describe labeled MAP4 (microtubule-associated protein 4) and MAP2 that can serve as an indicator of the localization (area), organization, and integrity of microtubules (page 30, paragraphs 0333-0334) which represent linear structures extending from a main body of a soma, as stated in the preamble of claims 1, 6, and 11. MAP2 is expressed specifically in neuronal cells (page 30, paragraph 0334) which is reasonably interpreted to be an indicator of the presence (area) of the linear structures of microtubules found in a neuron and extending from the main body of a soma, as stated in instant claims 5, 10, and 15. Sammak et al. describe processing images creating a cytoplasmic mask (where the microtubules exist) and nuclear mask (paragraphs 0215-0218) which represents deleting the linear structure from the image of the biological sample, as stated in the deleting steps of instant claims 6 and 11. Sammak et al. describe calculating cell-based

features and determining the number of spot objects in the cytoplasm or nucleus, including the number of nuclei as well as colony of cells, as well as a percentage of cells with a nuclear area above a threshold value (paragraphs 0213-0216) which represent measuring the image for a number of main bodies, or number of soma, as stated in the judging step of instant claims 6 and 11 and the condition pass/fail determining step and digitization step of instant claim 1. In Figure 9, Sammak et al. describe locating an object in a field (110) and if it does not meet valid cell criteria, then the rest of the current field is searched for unprocessed objects (113) which represents a changing of measuring area because previous area did not conform, as stated in instant claims 6 and 11. In Figure 9, if the current plate is not finished (114) then other wells are found (115) and the stage is advanced to the next well (116) which also represents a changing in measuring area, as stated in claims 6 and 11.

Wilhelm et al. state if a particular slide is anomalous, or if the automated cytology system did not operate effectively on the slide, it would be desirable to flag the unacceptable machine condition or slide characteristic so that potentially false results are not used (col. 1, lines 25-30). Wilhelm et al. state that various modifications could be made to their invention without departing from the scope of the invention (col. 8, lines 31-36). Sammak et al. state their invention is in the field of fluorescence-based cell and molecular biochemical assays for drug discovery (page 1, paragraph 0002). Sammak et al. state that drug discovery is a slow and costly process (page 1, paragraph 0004). Sammak et al. state it is necessary to provide new technologies to rapidly screen disease associated sequences to establish biological function to improve target validation and candidate optimization in drug discovery (page 1, paragraph 0005). Sammak et al. state there is a need to acquire, manage, and search multi-dimensional information

from cells (page 1, paragraph 0006). It would have been obvious to one of ordinary skill in the art at the time the invention was made to make improvements to drug discovery techniques of drug targets, as stated by Sammak et al., by automating cytology scoring and eliminating false results, as stated by Wilhelm et al., because this would provide higher throughput tools of extracting multiple parameter information in automated systems, as stated by Sammak et al. (page 1, paragraph 0006). Therefore, it would have been obvious to one of ordinary skill in the art to improve efficiency of cytology automated procedures for determining suitability of slides, as stated by Wilhelm et al. by miniaturizing methods involving nerve cells and other drug targets, as stated by Sammak et al., in order to improve drug discovery with increased throughput while decreasing volumes of reagents and test compounds required in each assay, as stated by Sammak et al. (page 1, paragraph 0006).

Thus, Wilhelm et al., in view of Sammak et al., make obvious the claims in the instant invention.

Applicant summarizes the Sammak et al. invention. Applicant states Sammak et al. do not describe the limitations that "deletes a linear structure of a cell having the linear structure extending from a main body of a soma from an image of a biological sample and determines whether a measuring area set as a numerical data acquiring area in the image of the biological sample has a number of main bodies, as a number of somas, that meets, a predetermined condition for acquiring numerical data". This statement is found unpersuasive as the masking steps described in the Sammak et al. reference represent a deletion of linear structures from the image before measurements are taken. Applicant states a person having ordinary skill in the art

at the time of the invention would not have been motivated to combine the references that would result in the instant invention. This statement is found unpersuasive as improving efficiency to speed up otherwise slow and costly processes, as stated by Sammak et al., represents proper motivation to combine references. Furthermore, Applicant has failed to provide any substantive reasoning as to why such motivation to combine references would be considered improper. Thus, Applicant's arguments are deemed unpersuasive.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform to the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

March 16, 2005

Marjorie A. Moran
3/16/05

MARJORIE A. MORAN
PRIMARY EXAMINER